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SCIENTIFIC COMMITTEE ON CONSUMER PRODUCTS

SCCP

Opinion on

TRICLOSAN

COLIPA N° P 32

Adopted by the SCCP
during the 9th plenary meeting of 10 October 2006

TABLE OF CONTENTS

1. BACKGROUND

Triclosan (INN) with the chemical name 2,4,4'-trichloro-2'-hydroxy-dipenylether is regulated in the Cosmetic Directive 76/768/EEC, Annex VI, part 1, reference no 25 and can therefore be used as a preservative up to a maximum concentration of 0.3% in the finished cosmetic product.

Preservatives are substances that may be added to cosmetic products for the primary purpose of inhibiting the development of micro-organisms in such products. Recently published reports have raised the question whether Triclosan could be involved in the development of bacterial resistance.

By 1st July 1986 the Scientific Committee on Cosmetology (SCC) expressed its opinion concerning certain preservatives including Triclosan. The opinion was based on the information available from public data (datasheets from National Institute of Public Health, the Netherlands, Council of Europe and TOXLINE).

In the submission from the Swedish Medical Products Agency in 2001 they requested a re-evaluation of Triclosan with respect to the risk of resistance development. Additionally they mentioned that an evaluation of the persistence of Triclosan in the environment was needed.

The Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP) adopted during the 21st Plenary Meeting of 17th September 2002 an opinion (SCCNFP/0600/02) concerning Triclosan with the conclusions and recommendations:

> "*In the light of conclusions and recommendations expressed in the opinion of the Scientific Steering Committee (SSC) on Triclosan resistance, adopted by the SSC at its meeting of 27-28 June 2002, and on the basis of the information provided by the Swedish Medical Products Agency, the SCCNFP is of the opinion that:*
>
> 1. *under current conditions of use of Triclosan as a preservative in cosmetic products, it is safe taking into account the risk of resistance by certain micro-organism.*
> 2. *there is no need for setting a new concentration limit for the use of Triclosan in cosmetic products.*
>
> *Taken into account the fact that Triclosan is used in other consumer products, the SCCNFP endorses the recommendations expressed by the SSC in its above-mentioned opinion and in its opinion on microbial resistance of 28 May 1999*."

The European Food Safety Authority (EFSA) has, on 15th March 2004, adopted an opinion on Triclosan used in food contact materials with the conclusion:

> "*The above-mentioned data do not affect the result of the previous evaluations. SCF_List: 3*[1] *Restriction: 5 mg/kg of food"*

[1] Substances for which an ADI or a TDI could not be established, but where the present use could be accepted.

The conclusion was followed by a "*Remark for Commission":*

- *Migration could exceed 5 mg/kg of food*
- *The use of this substance should not lead to a lowering of hygienic standards in food handling*
- *The Fat(consumption) Reduction Factor is not applicable despite log Po/w = 4.8, because migration in aqueous simulants may be higher than 10 % of the SML allocated to this substance, i.e. 5 ppm.*
- *Concerning efficacy, none of the data submitted demonstrated whether there is a significant effect on microbial numbers under in-use conditions of triclosan and to what extent the substance might contribute to reducing cross contamination.*
- *The Panel noted that no data were submitted to demonstrate activity against common food pathogens such as Campylobacter spp."*

EFSA mentioned herein, that toxicity was evaluated by the Scientific Committee on Food (SCF) in 2000 and not looked at in 2004.

The Commission has received a request from the Norwegian Authorities, Mattilsynet, in which they ask for a re-evaluation of the safety of the use of the preservative Triclosan in cosmetic products. The request from the Norwegian Authorities is based on an evaluation of Triclosan made by The Norwegian Scientific Committee for Food Safety in January 2005, with the conclusion:

- *"Widespread use of triclosan, including in cosmetic products, select for development of triclosan resistance,*
- *Furthermore, such use represents a public health risk in regard to development of concomitant resistance to clinically important antimicrobial agents,*
- *The assessment regarding use of triclosan in consumer products from 2000 (57)*[2] *seems strengthened by new evidence*"

Meanwhile COLIPA[3] made submission II only on bacterial resistance, considering from their point of view that re-evaluation of the general toxicological profile was not needed.

2. TERMS OF REFERENCE

1. Does SCCP consider a continued use of Triclosan as a preservative in cosmetic products as safe taking into account the new provided documentation of resistance development by certain micro-organisms and cross-resistance?

2. Does SCCP consider a continued use of Triclosan as a preservative in cosmetic products as safe for the consumer at the current concentration limit of maximum 0.3% taking into account the provided toxicological data?

[2] (57) refers to reference 57 in the evaluation done by The Norwegian Scientific Committee for Food Safety

[3] COLIPA - The European Cosmetic Toiletry and Perfumery Association

3. OPINION

Triclosan is regulated in the Cosmetic Directive 76/768/EEC, Annex VI, part 1, reference n° 25 and can therefore be used as a preservative up to a maximum concentration of 0.3% in the finished cosmetic product. Preservatives are substances that may be added to cosmetic products for the primary purpose of inhibiting the development of micro-organisms in such products. Moreover, Triclosan is marked with the symbol (+) and thus may be added to cosmetic products in concentrations other than those laid down in this Annex for other specific purposes apparent from the presentation of the product. Triclosan is used in oral hygiene products to control the accumulation of the dental plaque and in products intended for epicutaneous application.
In recent years, there have been general questions as to whether Triclosan and other biocides could be involved in the development of bacterial cross-resistance (1-5, 12).

Name of the substance: 2,4,4'-Trichloro-2'-hydroxydiphenyl ether (Triclosan).

CAS number: 3380-34-5.

Description of Triclosan

Triclosan is a synthetic, broad-spectrum antimicrobial agent. It has been available on the market since 1965. Medical uses of it include: i) eradication of methicillin-resistant *Staphylococcus aureus* (MRSA) in patients by reducing skin colonization (15); ii) skin and wounds disinfection; iii) in oral hygiene products to control dental plaque accumulation and gingivitis. It is also used in a wide variety of cosmetic products, fabrics, plastics and other products to prevent deterioration due to microbes.
Triclosan possesses antibacterial properties and also some antifungal and antiviral properties. It is marketed under diverse registered names, including *Microban* (when used in plastics and clothing), *Biofresh* (on acrylic fibres), *Irgasan DP-300* (cosmetics), *Lexol 300, Ster-Zac, Cloxifenolum* and others (1).

Molecular target (How it works)

Triclosan acts by blocking the active site of the enoyl-acyl carrier protein reductase enzyme (ENR), which is an essential enzyme in fatty acid synthesis in bacteria. By blocking the active site, Triclosan inhibits the enzyme, and therefore prevents the bacteria from synthesizing fatty acid, which is necessary for building cell membranes, for keeping the selective permeability and for reproducing. Triclosan is a very potent inhibitor of ENR, and only low concentrations are needed for powerful bactericidal action (1, 8). Humans do not have this ENR enzyme.

Activity spectrum

Triclosan has activity against many, but not all, types of Gram-positive and Gram-negative bacteria. It is bacteriostatic at low concentrations, but higher concentrations are bactericidal. *Pseudomonas aeruginosa* is highly resistant due to its outer membrane exclusion properties (19), whereas methicillin-resistant *Staphylococcus aureus* strains (MRSA) are inhibited over a range of about 0.1–4 mg/l. Triclosan shows significant activity against some mycobacteria, but is not

sporicidal. Bacterial resistance can arise from several mechanisms: i) mutations; ii) overproduction of ENR; iii) impermeability of the bacterial envelopes and iv) efflux pumping. Whilst Triclosan resistance in laboratory experiments may be associated with antibiotic resistance, clinical and environmental surveys have not demonstrated a conclusive link between Triclosan usage and antibiotic resistance development (11).

Effectiveness

Under the appropriate settings and conditions, such as in hospitals to prevent hospital-acquired infections, Triclosan has been proven to be effective. But no current data demonstrate any extra health benefits from having antibacterial-containing cleansers in ordinary households. Those households that use antibacterial products do not have any reduced risk of infectious diseases. The Center for Disease Control and Prevention has stated that antibacterial soaps are not necessary in everyday use, and washing hands with ordinary soap and warm water is an effective way to prevent home infections (1).

Exposure data

The only available exposure data provided are: i) the exposure data submitted by COLIPA during the preparation of the SSC opinion (6) and ii) the exposure data in the Norway report (2, 3). However, an updated exposure study concerning the total extent and all current applications of Triclosan in consumer and industrial products at European level is lacking.

Predicting the emergence of biocide and antibiotic resistance

Antibiotic or biocide resistance occurs when sufficient mutations of a gene cause changes in the spectrum of antibiotic or biocide substrates that the gene product can act upon. It is generally assumed that bacteria rarely acquire resistance to biocides because of their broad spectrum of activity and action at several target sites. This is in contrast with antibiotics that have a very specific site of action which facilitates the emergence of resistance. Since the introduction of penicillin in the 1940's, microbes have evolved resistance to practically all antibiotics. Increasing evidence suggests that mechanisms inducing resistance to biocides may also provide cross-resistance for antibiotics. (ref.: 1, 8, 21)

However, we do not yet know how to predict antibiotic or biocide resistance. What is understood is that increased exposures increase the probability of generating antibiotic resistance. But, a great variability of resistance patterns among micro-organisms, antibiotics and environmental factors are recognized.

Bacteria resistant to Triclosan have been reported in diverse species and environments but are not a universal phenomenon (9, 10, 11, 12, 13, 14, 16, 17, 18). Although biocide resistance mechanisms are much less understood than antibiotic resistance mechanisms, the central mechanisms for Triclosan resistance concerns efflux pumping (11, 20).

There is poor evidence that resistance and cross-resistance of clinically important organisms have any relation to any use of triclosan.

4. CONCLUSION

1. Does SCCP consider a continued use of Triclosan as a preservative in cosmetic products as safe taking into account the new provided documentation of resistance development by certain micro-organisms and cross-resistance?

Recent scientific papers (1, 7, 13, 14) and European institutions reports (2, 3, 4, 5) have expressed concerns about the indiscriminate use of biocides including triclosan. These concerns have been based on experimental studies and the theoretical association between increased occurrence of antibiotic cross-resistance and the use of biocides, including triclosan. Although probable, this link has not been fully demonstrated (9, 18).

On the basis of the available data, the SCCP is of the opinion that there is presently no evidence of clinical resistance and cross-resistance occurring from the use of triclosan in cosmetic products.

Information is required on consumer exposure to triclosan from all sources, including cosmetic products.

2. Does SCCP consider a continued use of Triclosan as a preservative in cosmetic products as safe for the consumer at the current concentration limit of maximum 0.3% taking into account the provided toxicological data?

For a toxicological assessment of the safe use of triclosan, the SCCP requires a dossier to be submitted in which data is provided to all relevant exposure and toxicological end-points and conforming to currently accepted standards.
This should be regarded as a matter of urgency because triclosan has been identified in human milk of some European populations.

5. MINORITY OPINION

Not applicable

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